

1146-32

### Patients on Lipid-Lowering Therapy at the Time of a Myocardial Infarction Have Smaller Infarcts: Further Evidence to Suggest a Salutary Effect in Acute Coronary Syndromes

Herbert D. Aronow, Thomas McRae, Martin J. Quinn, Eric J. Topol, Michael Lincoff, Penny L. Houghtaling, Michael S. Lauer, *Cleveland Clinic Foundation, Cleveland, Ohio.*

**Background:** By virtue of their effects on thrombosis and the coronary micro- and macrovasculature, it is plausible that lipid-lowering agents (LLA) might reduce infarct size. **Methods:** We compared infarct size among patients in the GUSTO IIb and PURSUIT trials who were (n=1048) or were not (n=9672) on a LLA prior to an enrolling myocardial infarction (MI). A propensity analysis was used to match patients on the probability of LLA treatment prior to the index admission. **Results:** In the overall (n=10720) and propensity-matched (n=6568) cohorts, the median CK-MB level was significantly lower among patients who were on a LLA prior to admission (4.0 vs. 5.0 X ULN, p<0.0001 and 4.4 vs. 4.0, p=0.01, respectively). In the propensity-matched cohort, fewer patients on a LLA before their MI had a CK-MB  $\geq$  3X ULN (58 vs. 63%, Risk Ratio [RR] = 0.92, 95% CI 0.87-0.97, p=0.002). After adjusting for other potential confounders and the propensity score, LLA pre-treatment was associated with smaller infarct size (RR for CK-MB  $\geq$  3X ULN = 0.94, 95% CI 0.88-0.99, p = 0.04). **Conclusion:** Patients on a LLA prior to sustaining an MI had significantly smaller infarcts. These findings provide further evidence to suggest that lipid-lowering therapy may exert salutary effects in the setting of an acute coronary syndrome.

1146-33

### Nonselective Nonaspirin Nonsteroidal Antiinflammatory Medications Are Associated With Reduced Risk of Myocardial Infarction

Stephen E. Kimmel, Jesse A. Berlin, Muredach Reilly, Jane Jaskowiak, Lori Kishel, Brian L. Strom, *University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, Center for Clinical Epidemiology and Biostatistics, Philadelphia, Pennsylvania.*

**Background:** Non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit both cyclooxygenase-1 (COX-1) and COX-2 (i.e., nonselective NSAIDs) may reduce the risk of myocardial infarction (MI) through reversible inhibition of platelet function. Knowledge of the effects of nonselective NSAIDs on MI could aid in interpreting recent trials comparing nonselective NSAIDs with COX-2 inhibitors.

**Methods:** A case-control study of first MI, ages 40 through 75, was conducted among 36 hospitals in a 5-county area during a 26-month period in 1999-2001. Cases were patients hospitalized with a first MI, and controls were randomly selected from the same geographic area. Detailed information regarding NSAID use in the week before the MI for cases and before the interview for controls was collected via telephone interviews using state-of-the-art methods, including NSAID picture prompts. Nonselective NSAID use was compared with no use in the prior week. Multivariable logistic regression was used to adjust for age, sex, body mass index, family history, cigarette smoking, insurance, exercise, and history of coronary disease, heart failure, hypertension, hypercholesterolemia, diabetes, or arthritis. COX-2 inhibitor use during this time period was low and therefore not included.

**Results:** 909 cases (21% nonselective NSAID users in the prior week) and 3030 controls (34% nonselective NSAID users) were interviewed. There was a significant protective effect against MI for nonselective NSAID use in both the prior week [multivariable odds ratio (OR) 0.67, 95% confidence interval (CI): 0.54-0.82] and the prior 24 hours (multivariable OR 0.61, 95% CI: 0.46-0.80). However, there was a significant interaction between current aspirin (ASA) use (within the index week) and NSAIDs: NSAIDs were protective among those not using ASA (OR 0.56; 95% CI: 0.44-0.72), but were not protective among ASA users (OR 1.01; 95% CI: 0.69-1.47; interaction P<0.01).

**Conclusion:** Current use of nonselective NSAIDs is associated with a reduced odds of MI. Among ASA users, however, there is no effect of NSAID use on MI risk.

1146-34

### High Fasting Insulin Levels in Patients With Coronary Artery Disease and No Known Diabetes is a Potent Predictor of Future Cardiac Events

Michael Angiol, Pierre Theroux, *MONTREAL HEART INSTITUTE, MONTREAL, Quebec, Canada.*

**Background:** Hyperinsulinism is believed to be one mechanism contributing to coronary artery disease (CAD) in diabetic patients. However, the potential deleterious effect of hyperinsulinemia in non-diabetics has not yet been assessed.

**Methods:** A sub-population of non-diabetic patients was extracted from a prospective case-control cohort study that examine biological and genetic markers associated with CAD and subsequent prognosis. All patients included in this study had angiographically documented CAD. Major adverse cardiac events (MACE) recorded during 1-year FU were death, myocardial infarction (MI), myocardial revascularisation (either PTCA or CABG) and hospitalization for acute coronary syndrome (ACS).

**Results:** The study population included 303 non-diabetic patients (male 79%, age: 58  $\pm$  10 years). Risk factors in these patients were smoking in 83%, systemic hypertension in 39% and hypercholesterolemia in 77%, in addition prior MI, PTCA and CABG were present in 53%, 68% and 22% of patients, respectively. Biologic screening included, D-dimers, homocysteine, CRP, fibrinogen, Lp(a), folates and insulin plasma levels. During FU, 49 pts (16%) had at least 1 event (death 3, MI 5, ACS 18, myocardial revascularisation 40). Among the studied characteristics, insulin levels were the most potent and single independent predictor of MACE. Kaplan-Meier probabilities of survival without events were 87% in the low tertile of insulin (<50 pmole/L), 88% in the medium tertile (50 to 82 pmole/L) and 76% in the high tertile (>82 pmole/L) (low vs. high: RR=2.19, 95%CI 1.0-4.6, p<0.019 and medium vs. high: RR=2.4, 95%CI 1.1-5.1, p<0.016). Baseline levels of insulin correlated with fibrinogen (R=0.17, p<0.003) CRP (R=0.16, p<0.005) and body

mass index (R=0.4, p<0.0001).

**Conclusion:** Hyperinsulinemia in non-diabetic patients with CAD is associated with elevated inflammatory markers and is a strong predictor of future cardiac events.

1146-35

### Acute Myocardial Infarction and Renal Failure: Impact of Treatment on Short and Long-Term Survival

R. Scott Wright, Joseph G. Murphy, Charles A. Herzog, Guy S. Reeder, Wayne L. Miller, Stephen L. Kopecky, Robert C. Albright, Brent A. Williams, Allan S. Jaffe, *Mayo Clinic and Foundation, Rochester, Minnesota, University of Minnesota School of Medicine and Hennepin County Medical Center, Minneapolis, Minnesota.*

**Background:** Patients with severe renal failure have reduced survival following acute myocardial infarction (AMI). Few data are available about management of AMI in these populations including the impact of aggressive treatment on outcome following AMI.

**Methods:** We stratified 3205 patients with AMI by creatinine clearance (CC): CC>75 cc/min (n=965), CC 50-75 cc/min (n=919), CC 35-50 cc/min (n=694), CC<35 cc/min (n=694) and end stage renal disease (ESRD) on dialysis for at least one month prior to index AMI (n=46). We compared treatment strategies during the hospitalization for AMI and estimated the influence on treatment strategies with regard to in-hospital and long-term survival by CC.

**Results:** The use of aspirin, heparin and beta blockers were significantly higher in those with normal renal function compared to any degree of renal failure, all p<0.001. Acute reperfusion therapy was more frequently utilized in patients without renal failure (31.9%) compared to ESRD (6.5%), severe renal failure (13.0%), moderate renal failure (21.2%) and mild renal failure (25.2%), p<0.001. The influence of these therapies on survival is depicted (Table).

**Conclusions:** Patients with any degree of renal disease have increased mortality risks following AMI, and those with severe renal failure have similar survival to those with ESRD. The estimation CC at time of admission with AMI may help better identify patients with increased mortality risks.

#### Predictors of Mortality

In-Hospital Mortality			
Adjusted model results:	RR	CI	p-value
Killip Class (>1 vs 1)	2.65	(1.99, 3.53)	<0.001
Age (>75 vs <65)	1.64	(1.06, 2.52)	0.025
Age (65-75 vs <65)	1.45	(0.94, 2.24)	0.091
Diabetes	1.44	(1.05, 1.98)	0.024
Gender (female vs male)	0.73	(0.54, 0.97)	0.030
ACEI use w/in 24h of admit	0.40	(0.27, 0.60)	<0.001
Aspirin use w/in 24h	0.40	(0.30, 0.54)	<0.001
Post-Discharge Mortality			
Adjusted model results:	RR	CI	p-value
Age (>75 vs <65)	2.86	(2.14, 3.83)	<0.001
Killip class (>1 vs 1)	1.80	(1.51, 2.15)	<0.001
Age (65-75 vs <65)	1.78	(1.33, 2.37)	<0.001
Stroke	1.71	(1.41, 2.08)	<0.001
Diabetes	1.39	(1.15, 1.68)	<0.001
Prior MI	1.34	(1.12, 1.60)	0.002
Aspirin use at d/c	0.65	(0.53, 0.80)	<0.001
$\beta$ -blocker use at d/c	0.72	(0.61, 0.86)	<0.001
Primary Reperfusion	0.73	(0.58, 0.92)	0.007

1146-36

### Bradycardia, Hypotension, and Chronotropic Incompetence Are Common With Acute Proximal Versus Distal RCA Occlusion

James A. Goldstein, Daniel T. Lee, Terry Bowers, Cindy L. Grines, Mark Pica, William W. O'Neill, *William Beaumont Hospital, Royal Oak, Michigan.*

**Background:** Bradycardia and hypotension commonly complicate inferior MI and are thought to be mediated by Bezold-Jarisch reflexes arising from the ischemic LV inferior wall. Pts with RV infarction due to proximal RCA occlusion (occlx) are especially prone to bradycardia and hypotension, although the reasons for this proclivity have not been delineated. We hypothesized that proximal vs distal occlx of the RCA plays a role. **Methods:** In 205 pts with IMI undergoing 1<sup>o</sup> PTCA, we defined the location of RCA occlx as proximal to the RV branches or distal to the RV branches but compromising the LV branches. We analyzed charts for the development of bradycardia (<50/min), hypotension (syst BP<90 mm Hg) and bradycardia-hypotension (syst BP<90 + HR<50). **Results:** We identified proximal RCA occlx in 163(76%) pts and distal occlx in 52(24%) others. Compared to those with distal occlx, pts with proximal occlx more frequently developed bradycardia (23 vs 10%, p=.05); and hypotension (45 vs 29%, p=.01). Interestingly, in pts with prox occlx developing hypotension, whereas frank bradycardia (<50/min) occurred in 32% of cases, the heart rate was <100 in 94% of such patients, such lack of compensatory sinus tachycardia indicative of chronotropic incompetence. **Conclusions:** These results indicate that acute proximal RCA occlx compromising flow to the RV branches as well as the LV inferior wall commonly results in hypotension with chronotropic incompetence, as well as frank bradycardia. These phenomenon are less common with distal occlx inducing LV ischemia alone, suggesting that reflex mechanisms originating from the ischemic right heart may play a mechanistic role.